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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

DIBRINO, MARIANNE NMN

ART UNIT PAPER NUMBER

1644

DATE MAILED: 09/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/759,207

Applicant(s)

PECKER ET AL.

Examiner

DiBrino Marianne

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 May 2004 and 21 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/13/04 has been entered.
2. Applicant's amendment filed 1/21/04 is acknowledged and has been entered.
3. The amendment filed 1/21/04 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amendment to insert a complete paragraph before line 1 on page 20 of the instant specification with regard to a polypeptide having heparanase activity which shares at least 65%, 75%, 85% or 95% homology with SEQ ID NO: 2.
4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 15-19 and 22-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendatory material not supported by the specification and claims as originally filed is as follows: an isolated antibody specifically binding or elicited by at least one epitope of a mammalian heparanase protein, said heparanase protein being at least 65%, at least 75%, at least 85% or at least 95% homologous to SEQ ID NO: 2.

6. Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the

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inventor had possession at that time of the . . . claimed subject matter", Vas-Cath, Inc. v. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed antibody specifically binding to or elicited by at least one epitope of a mammalian heparanase protein, said heparanase protein being at least 80% or at least 90% homologous to SEQ ID NO: 2.

The instant claims encompass antibodies to proteins that are specific for or elicited by heparanases of undisclosed structure. The said antibodies can be specific for or elicited by any heparanase protein with at least 65%, 70%, 75%, 80%, 85%, 90% or 95% homology to SEQ ID NO: 2. In addition, the instant claims that recite "elicited by at least one epitope of a mammalian heparanase protein" encompass antibodies that are elicited by a portion of a mammalian heparanase protein, but that may not bind specifically to the said heparanase protein, i.e., it is elicited towards an epitope not specific to the said heparanase. There is insufficient disclosure in the specification for said antibodies.

The specification discloses that anti-heparanase antibodies can be produced against heparanases that have widely disparate amino acid sequences, for example those cited on page 12 at lines 13-16 of the instant application, i.e., mouse B16-10 heparanase, human platelet heparanase, heparanases produced by several human tumor cell lines and CHO cells.

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. However, a generic statement such as antibodies specific for or elicited by heparanase protein with at least 65%, 70%, 75%, 80%, 85%, 90% or 95% homology to SEQ ID NO: 2, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of being specific for or elicited by a protein with at least 65%, 70%, 75%, 80%, 85%, 90% or 95% homology to SEQ ID NO: 2 and having heparanase activity. It does not specifically define any of the compounds that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others, other than that they are specific for or elicited by heparanases that are at least 65%, 70%, 75%, 80%, 85%, 90% or 95% homologous to SEQ ID NO: 2. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. In addition, a definition by function and in the instant case by partial structure where the activity is not correlated with a specific structural feature, does not suffice to define the genus because it is only an indication of what the property the heparanase protein has, rather than what it is. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many such species may achieve that result. The description requirement of the patent

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statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

One of ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

Applicant's arguments in the amendment filed 1/21/04 have been fully considered, but are not persuasive.

Applicant's position in the said amendment is of record on pages 7-11.

It is the Examiner's position in response to the said arguments, including in response to Applicant's position that the present claims function in the same manner as a Markush group for a molecule or a chemical entity because they define the genus of heparanase proteins according to the characteristic of homology (i.e., the lowest percentage being 60%) of a defined degree relative to a defined sequence (i.e., SEQ ID NO: 2), i.e., that the defined sequence acts as the equivalent of a chemical backbone and the percentage homology acts as the functional groups as it determines any permissible variations on the backbone structure, that although a partial structure is recited in terms of % homology to SEQ ID NO: 2, there is no disclosure of structure- function relationship, i.e., "complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure" (see MPEP 2163) such as where the heparanase bindings sites are in heparanase proteins, what their sequences are or what local homology those sites possess, and/or what other portions of SEQ ID NO: 2 are required for function in addition to heparanase binding sites. In Applicant's amendment filed 5/27/03, in the sequences in Appendix A for several heparanases, the heparanase binding sites are not in the same position in the proteins, the said binding sites are not the same sequences, and the degree of homology of each of human, rat, mouse and chicken heparanase sequences detailed in the said Appendix A is not disclosed in the instant specification. In addition, instant claim 2 recites "wherein said heparanase protein is native", i.e., wherein the heparanase protein is a natural homolog or allele of SEQ ID NO: 2, in any mammal, including in mammals that may not possess a heparanase protein homolog of SEQ ID NO: 2. In addition, the instant claims encompass any variant of SEQ ID NO: 2, including deletion or substitution variants that retain function.

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7. Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

The specification does not disclose how make and or/use claimed antibody specifically binding to or elicited by at least one epitope of a mammalian heparanase protein, said heparanase protein being at least 65%, 70%, 75%, 80%, 85%, 90% or 95% homologous to SEQ ID NO: 2. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass antibodies to proteins that are specific for or elicited by heparanases of undisclosed structure. The said antibodies can be specific for or elicited by any heparanase protein with at least 65%, 70%, 75%, 80%, 85%, 90% or 95% homology to SEQ ID NO: 2 which is 543 amino acid residues in length. In addition, the instant claims that recite "elicited by at least one epitope of a mammalian heparanase protein" encompass antibodies that are elicited by a portion of a mammalian heparanase protein, but that may not bind specifically to the said heparanase protein, i.e., it is elicited towards an epitope not specific to the said heparanase. There is insufficient disclosure in the specification for said antibodies.

The specification discloses that anti-heparanase antibodies can be produced against heparanases that have widely disparate amino acid sequences, for example those cited on page 12 at lines 13-16 of the instant application, i.e., mouse B16-10 heparanase, human platelet heparanase, heparanases produced by several human tumor cell lines and CHO cells.

There is no disclosure in the instant specification as to which amino acid residues at which positions comprise heparanase binding sites, which amino acid residues at other positions are tolerant of allowing the heparanase binding sites to function. Applicant presents examples in Appendix A of Applicant's amendment filed 5/27/03 for several heparanases of different sequence and the heparinase binding sites are not in the same position in the proteins and the said binding sites are not the same sequences.

The predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain function and properties requires a knowledge of, and guidance with regard to which amino acid residues at which positions in the amino acid sequence, if any are tolerant to modification and which are intolerant to modification, and detailed knowledge of the ways in which the product's structure relates to its function. Evidentiary reference Zhou et al (PNAS USA 1998, 95: 2492-7, previously provided) teaches that a single amino acid substitution in the HFE causes profound changes in the regulation of iron homeostasis in humans.

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The literature reports numerous examples of structurally related polypeptide families wherein individual members have distinct, and sometimes even opposite, biological activities. For example, Tischer et al (U.S. Patent 5,194,596) establishes that VEGF (a member of the PDGF family displaying a high degree of global homology with naturally occurring PDGF) is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells, which is opposite to the mitogenic activity of naturally occurring PDGF which is mitogenic for vascular smooth cells but not for vascular endothelial cells (column 2, line 46 to column 3, line 2). The differences between PDGF and VEGF are also seen in vivo, wherein endothelial pericyte associations in the eye are disrupted by intraocular administration of PDGF but accelerated by intraocular administration of VEGF (Benjamin et al., 1998, Development 125: 1591-1598; see Abstract and pp. 1594-1596). In the transforming growth factor (TGF) family, Vukicevic et al (Proc. Natl. Acad. Sci. USA, Vol. 93, 1996, pages 9021-9026) disclose that OP-1, a member of the TGF- β family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF- β family members BMP-2 and TGF- β 1 had no effect on metanephrogenesis under identical conditions (especially page 9023, paragraph bridging columns 1-2). See also Massague, who reviews other members of the TGF- β family (1987, Cell 49: 437-8, especially p. 438, column 1, second full paragraph to the end). OP-1, BMP-2 and TGF- β 1 all display a high degree of global homology with one another. Similarly, PTH and PTHrP are two structurally related proteins which can have opposite effects on bone resorption (Pillbeam et al, Bone, Vol. 14, 1993, pages 717-720, especially page 717, second paragraph of Introduction). Kopchick et al (U.S. Patent No. 5, 350, 836) discloses several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by a single amino acid residue (column 2, lines 37-48).

Generally, the art acknowledges that function cannot be predicted based on structural similarity to a protein found in the sequence databases. For example, Skolnick et al (2000, Trends in Biotech. 18: 34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10: 398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are echoed by Doerks et al (1998, Trends in Genetics 14: 248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) over-predictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al (1997, Nature Biotechnology 15: 1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15: 132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major

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gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Bork et al (1996, Trends in Genetics 12: 425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts. Finally, Bowie et al (Science, Vol. 247, 1990, pages 1306-1310) state that determination of three dimensional structure from primary amino acid sequence, and the subsequent inference of detailed aspects of function from structure is extremely complex and unlikely to be solved in the near future (especially page 1306).

Therefore, the problem of predicting functional aspects of the polypeptide product from mere sequence data of polypeptides being at least 65%, 70%, 75%, 80%, 85%, 90% or 95% homologous to SEQ ID NO: 2" and what changes can be tolerated is complex and well outside the realm of routine experimentation.

There is insufficient guidance in the specification as to how to make and/or use the instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

Applicant's arguments in the amendment filed 1/21/04 have been fully considered but are not persuasive.

Applicant's arguments are of record in the said amendment on pages 1-17.

It is the Examiner's position with regard to Applicants arguments in the said amendment:

(1) Wands factor 1: Undue experimentation and Wands factor 2: amount of direction or guidance presented in the specification

It is the Examiner's position that although guidance is provided in the instant specification for determining % homology, for preparing a protein of a defined sequence and for testing for heparanase activity, that disclosure is not provided that relates to which portions of SEQ ID NO: 2 are required for heparanase function and the arguments enunciated in the instant rejection apply hereto.

(2) Wands factor 3: Presence or absence of working examples

It is the Examiner's position that Applicant's working example is SEQ ID NO: 2, a 543 amino acid residue long protein.

(3) Wands factor 4: Nature of the invention

It is the Examiner's position that proteins are chemical entities is not in dispute in the instant rejection.

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(4) Wands factor 5: The state of the Prior Art

It is the Examiner's position that although "routine cookbooks for molecular biology existed at the time of filing, the arguments enunciated at "(1)" and in the instant rejection apply hereto.

(5) Wands factor 6: Relative skill of those in the art

It is the Examiner's position that the relative skill in the art can be high, but that the arguments at "(1)" and in the instant rejection apply hereto.

(6) Wands factor 7: Predictability or unpredictability in the art

It is the Examiner's position that the Applicant's assertion that molecular biology is more unpredictable than chemistry is not the issue under discussion, and that the arguments at "(1)" and in the instant rejection apply hereto.

(7) Wands factor 8: The breadth of the claims

It is the Examiner's position that the claims encompass an antibody specifically binding to or an antibody elicited by a mammalian heparanase protein with up to 40% dissimilarity to SEQ ID NO: 2, a 543 amino acid residue long protein. In addition, the claims that recite wherein the said antibody can be one that is elicited by at least one epitope of a mammalian heparanase protein encompass antibodies that are elicited by a portion of a mammalian heparanase protein, but that may not bind specifically to the said heparanase protein, i.e., it is elicited towards an epitope not specific to the said heparanase. Applicant mentions an attached affidavit that attests to degree of cross-reactivity between antibody isotypes of different species, however no such affidavit has been received. In any case, it is the Examiner's position that the degree of homology within the heavy chain of antibody isotypes between species is not relevant to the discussion of degree of homology to SEQ ID NO: 2, a heparanase protein. Applicant argues that the amino acid sequence of the target binding site is not of major significance per se, since the antibodies (presumably to chick, human platelet, tumor cell line and CHO cell heparanases) do not recognize linear chains, but 3-dimensional structures, and that it is not relevant where the heparanase binding sites are situated. It is the Examiner's position that 3 dimensional structure is more difficult to predict than linear conformation, and that the issue is not where the heparanase binding sites are situated so that the antibodies can bind to them, but rather how to design a protein with at least 60% homology to SEQ ID NO: 2 that will maintain heparanase activity. It is the Examiner's position that the arguments enunciated in the instant rejection apply hereto.

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8. For the purpose of prior art rejections, the filing date of the instant claims 15-19 and 22-25 is deemed to be the filing date of the instant application, i.e. 1/16/01, as the parent applications do not support the claimed limitations, i.e., "being at least" 65%, 75%, 85% or 95% homologous to SEQ ID NO: 2", of the instant application.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 15-19 and 22-25 are rejected under 35 U.S.C. 102(b) as being anticipated by A-Geneseq Accession Number AAY17083.

A-Geneseq Accession Number AAY17083 teaches specific antibodies to heparanase protein being 96.3% similar to SEQ ID NO: 2 of the instant claims.

With regard to the recitation of "homologous" in the instant claims, the disclosure in parent application serial no. 08/922,170 on page 28 at lines 15-19 is that the sequence analysis software package developed by the GCG at University of Wisconsin disclosed was used to perform database searches for sequence similarity. Therefore the claimed antibody appears to be the same or similar to the antibody of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on applicant to show an unobvious distinction between the antibody of the instant invention and that of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

11. Claims 15-19 and 22-25 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 9921975 A1.

WO 9921975 A1 teaches specific antibodies to heparanase protein (SEQ ID NO: 15 of the said WO document) being 96.3% similar to SEQ ID NO: 2 of the instant claims.

With regard to the recitation of "homologous" in the instant claims, the disclosure in parent application serial no. 08/922,170 on page 28 at lines 15-19 is that the sequence analysis software package developed by the GCG at University of Wisconsin disclosed was used to perform database searches for sequence similarity. Therefore the claimed antibody appears to be the same or similar to the antibody of the prior art absent a showing of unobvious differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on applicant to show an unobvious distinction between the antibody of the instant invention and that of the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

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12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 10-27 of U.S. Patent No. 6,562, 950 B2 in view of Hoogewerf et al (J. Biol. Chem. 270/7: 3268-3277, 1995) and U. S. Patent No. 5,206,223 and Bendig (METHODS: A Companion to Methods in Enzymology, 8: 83-93, 1995).

The heparanase protein SEQ ID NO: 2 recited in the instant claims is 100% similar to SEQ ID NO: 1 recited in the claims of U.S. Patent No. 6,562, 950 B2, and the instant claims encompass the monoclonal antibody/pharmaceutical composition thereof claimed by U.S. Patent No. 6,562, 950 B2. Although the instant claims do not recite humanized or human monoclonal antibody, nor wherein the anti-heparanase antibody specifically inhibits heparanase activity, nor wherein the monoclonal antibody binds to a C-terminal portion of heparanase, Hoogewerf et al teach antibodies to the C-terminal portion of a putative heparanase protein was useful in inhibiting heparanase activity, U.S. Patent No. 5,206,223 discloses that inhibiting heparanase activity is useful for preventing or delaying allograft rejection or alleviating and treating an autoimmune disease such as arthritis, and Bendig teaches humanization of antibodies from non-human species such as rodents in order to reduce immunogenicity in humans. The antibodies recited in the instant application as well as in U.S. Patent No. 6,562, 950 B2 are specific for human heparanase. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to humanize the antibody of the instant claims, to make the antibody against the C-terminal portion of the heparanase, and to make a neutralizing antibody. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to inhibit heparanase activity in humans.

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14. Claims 15-19 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,562, 950 B2.

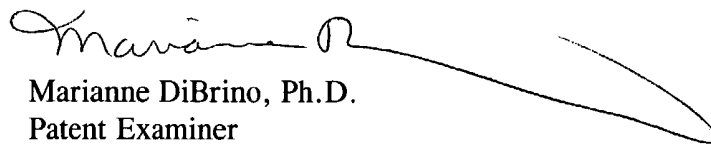
U.S. Patent No. 6,562, 950 B2 discloses monoclonal and polyclonal antibodies elicited against and binding to a human heparanase protein having 100%, i.e., at least 95%, 85%, 75% or 65%, similarity to the heparanase protein SEQ ID NO: 2 recited in the instant claims.

15. No claim is allowed.


16. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Wednesday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Chan Y Christina, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
September 1, 2004



CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600